AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

1. (Currently amended): A bioreactor for cultivating living cells in a liquid medium comprising:
   (a) a first substrate having a first surface and an opposite second surface, defining a chamber therebetween for receiving the cells and the liquid medium;
   (b) a barrier dividing the chamber into a first subchamber and a second subchamber, wherein the barrier has a porosity to allow the first subchamber and the second subchamber in fluid communication and allow at least one predetermined type of cells to permeate between the first subchamber and the second subchamber;
   (c) a second substrate positioned adjacent to the first surface of the first substrate;
   (d) a third substrate, wherein the third substrate is positioned adjacent to the second surface of the first substrate; and
   (e) means positioned in the third substrate and adapted for electrochemical measurements of the cells responsive to the liquid medium in at least one of the first subchamber and the second subchamber.

2. (Original): The bioreactor of claim 1, wherein the first subchamber is adapted for receiving a first type of material and the second subchamber is adapted for receiving a second type of material.

3. (Original): The bioreactor of claim 2, wherein each of the first type of material and the second type of material contains at least one selected from the group of cells, chemicals, and fluids.

4. (Original): The bioreactor of claim 3, wherein the cells comprise bacteria.

5. (Original): The bioreactor of claim 3, wherein the cells comprise protozoa.

6. (Original): The bioreactor of claim 1, further comprising a biocompatible coating layer applied to the chamber walls.

7. (Original): The bioreactor of claim 6, wherein the biocompatible coating layer comprises a material that may inhibit cell adhesion to the biocompatible coating layer, enhance cell adhesion to the biocompatible coating layer, or function as a fluorescent marker or indicator of the state of cells.

8. (Original): The bioreactor of claim 1, further comprising at least one inlet port and an input transfer channel in fluid communication with the inlet port and one of the first subchamber and the second subchamber for allowing delivery of the cells, fluids or chemicals to the corresponding subchamber.

9. (Original): The bioreactor of claim 8, further comprising at least one outlet port and an outlet transfer channel in fluid communication with the outlet port and one of the first subchamber and the second subchamber for allowing removal of the cells, fluids or chemicals from the corresponding subchamber.

10. (Original): The bioreactor of claim 9, further comprising at least one auxiliary port and an auxiliary channel in fluid communication with the auxiliary port and one of the input transfer channel and the outlet transfer channel for flushing the corresponding transfer channel.

11. (Original): The bioreactor of claim 10, further comprising at least one access port and an access channel in fluid communication with the access port and one of the first subchamber and the second subchamber for allowing delivery or removal of the cells, fluids, chemicals, coating material or sensing material to the corresponding subchamber.

12. (Currently amended): The bioreactor of claim 11, ~~further comprising a second substrate,~~ wherein the second substrate ~~is positioned adjacent to the first surface of the first substrate and~~ defines a plurality of connection channels, each of the connection channels being formed so as to be in fluid communication with a corresponding one of the inlet port, the outlet port, the auxiliary port, and the access port.

13. (Original): The bioreactor of claim 12, further comprising a plurality of connection ports, each of the connection ports being formed with a channel and being positioned to the second substrate such that each channel of the connection ports is in fluid communication with a corresponding one of the connection channels formed in the second substrate.

14. (Original): The bioreactor of claim 1, wherein the first substrate is fabricated from glass, Mylar, PDMS, silicon, a polymer, a semiconductor, or any combination of them.

15. (Original): The bioreactor of claim 1, wherein the barrier comprises a porous material.

16. (Original): The bioreactor of claim 1, wherein the barrier is microfabricated so as to form a structure allowing the fluid communication between the first subchamber and the second subchamber.

17. (Canceled).

18. (Canceled).

19. (Currently amended): The bioreactor of claim ~~18~~ 1, wherein the means for electrochemical measurements comprises:

(i) a reference electrode;

(ii) a counter electrode;

(iii) a plurality of edge connector pads; and

(iv) a plurality of electrically conductive leads, where a first electrically conductive

lead electrically couples the reference electrode to a corresponding edge connector pad, and a second electrically conductive lead electrically couples the counter electrode to a corresponding edge connector pad.

20. (Original): The bioreactor of claim 19, wherein the means for electrochemical measurements further comprises:

a plurality of individually addressable working electrodes, each being electrically coupled to a corresponding edge connector pad through a corresponding electrically conductive lead.

21. (Currently amended): The bioreactor of claim 20, wherein the liquid medium comprises at least one analyte, and wherein the plurality of individually addressable working electrodes are adapted for ~~capable of~~ sensing the concentration of a single analyte of the liquid medium at multiple locations in the chamber or the concentrations of a plurality of analytes of the liquid medium at multiple locations in the chamber at a time period shorter than a characterization reaction time related to at least one of cellular physiological activities of the cells.

22. (Currently amended): The bioreactor of claim 21, wherein the plurality of individually addressable working electrodes are further adapted for ~~capable of~~ measuring the metabolic variables related to the cells responsive to the liquid medium at multiple locations in the chamber at a time period shorter than a characterization reaction time related to at least one of cellular physiological activities of the cells.

23. (Currently amended): The bioreactor of claim ~~17~~ 1, wherein the third substrate comprises a semiconductor material.

24. (Original): The bioreactor of claim 23, wherein the semiconductor material comprises silicon.

25. (Original): The bioreactor of claim 1, further comprising a fourth substrate, wherein the fourth substrate is positioned above the second surface of the first substrate.

26. (Original): The bioreactor of claim 25, further comprising means positioned in the fourth substrate and adapted for optical measurements of the cells responsive to the liquid medium in at least one of the first subchamber and the second subchamber.

27. (Original): The bioreactor of claim 26, wherein the means for optical measurements comprises:

(i) a plurality of optical sensors;

(ii) a plurality of edge connector pads; and

(iii) a plurality of optically conductive leads, each optically coupling an optical sensor to a corresponding edge connector pad.

28. (Original): The bioreactor of claim 26, wherein the plurality of optical sensors comprises at least one device selected from the group of an LED and photodiode pair, a fiber optic coupler, and an optical detecting head.

29. (Currently amended): The bioreactor of claim 28, wherein the liquid medium comprises at least one analyte, and wherein the plurality of optical sensors are adapted for ~~capable of~~ sensing the concentration of a single analyte of the liquid medium at multiple locations in the chamber or the concentrations of a plurality of analytes of the liquid medium at multiple locations in the chamber at a time period shorter than a characterization reaction time related to at least one of cellular physiological activities of the cells.

30. (Currently amended): The bioreactor of claim 29, wherein the plurality of optical sensors are further adapted for ~~capable of~~ measuring the metabolic variables related to the cells responsive to the liquid medium at multiple locations in the chamber at a time period shorter than the characterization reaction time related to at least one of cellular physiological activities of the cells.

31. (Original): The bioreactor of claim 25, wherein the fourth substrate comprises a semiconductor material.

32. (Original): The bioreactor of claim 31, wherein the fourth substrate is at least partially transparent.

33. (Currently amended): A bioreactor for cultivating living cells in a liquid medium comprising:

(a) a substrate having a first surface and an opposite second surface, defining a chamber therebetween for receiving the cells and the liquid medium, wherein the chamber is formed with a center and a boundary;

(b) a first barrier enclosing the center and a portion of the chamber to form a central chamber; ~~and~~

(c) a second barrier positioned between the first barrier and the boundary so as to form an intermediate chamber and an outer chamber; and

(d) means adapted for electrochemical measurements of the cells responsive to the liquid medium in at least one of the outer chamber, the intermediate chamber and the central chamber,

wherein the first barrier has a first porosity to allow the central chamber and the intermediate chamber in fluid communication and allow at least a first predetermined type of cells to permeate between the central chamber and the intermediate chamber, and the second barrier has a second porosity to allow the outer chamber and the intermediate chamber in fluid communication and allow at least a second predetermined type of cells to permeate between the outer chamber and the intermediate chamber.

34. (Original): The bioreactor of claim 33, wherein the central chamber is adapted for receiving a first type of material, the intermediate chamber is adapted for receiving a second type of material, and the outer chamber is adapted for receiving a third type of material.

35. (Original): The bioreactor of claim 34, wherein each of the first type of material, the second type of material and the third type of material contains at least one selected from the group of cells, chemicals, and fluids.

36. (Original): The bioreactor of claim 33, wherein the first predetermined type of cells comprises tumor cells, which normally is received in the central chamber corresponding to a tumor space.

37. (Original): The bioreactor of claim 36, wherein the second predetermined type of cells comprises normal tissue cells, which normally is received in the intermediate chamber corresponding to a tissue space.

38. (Original): The bioreactor of claim 37, wherein the outer chamber is corresponding to a vascular space adapted for receiving endothelial cells, macrophage cells, neutophil cells, any combination of them, or other immune cell type.

39. (Original): The bioreactor of claim 33, further comprising a biocompatible coating layer applied to the chamber walls at the boundary.

40. (Original): The bioreactor of claim 39, wherein the biocompatible coating layer comprises a material that may inhibit cell adhesion to the biocompatible coating layer, enhance cell adhesion to the biocompatible coating layer, or function as a fluorescent marker or indicator of the state of cells.

41. (Original): The bioreactor of claim 33, further comprising at least one inlet or outlet port and an input or output transfer channel in fluid communication with the inlet or outlet port and the external chamber for allowing delivery of the cells, fluids or chemicals to the outer chamber.

42. (Original): The bioreactor of claim 41, further comprising at least one inlet or outlet port and an input or output transfer channel in fluid communication with the inlet or outlet port and the central chamber for allowing delivery of the cells, fluids or chemicals to the central chamber.

43. (Original): The bioreactor of claim 42, further comprising at least one inlet or outlet port and an input or output transfer channel in fluid communication with the inlet or outlet port and the intermediate chamber for allowing delivery of the cells, fluids or chemicals to the intermediate chamber.

44. (Original): The bioreactor of claim 33, wherein the substrate is fabricated from glass, Mylar, PDMS, silicon, a polymer, a semiconductor, or any combination of them.

45. (Original): The bioreactor of claim 33, wherein the first barrier comprises a porous material.

46. (Original): The bioreactor of claim 45, wherein the first barrier is microfabricated so as to form a first structure allowing the fluid communication between the central chamber and the intermediate chamber.

47. (Original): The bioreactor of claim 46, wherein the second barrier comprises a porous material.

48. (Original): The bioreactor of claim 47, wherein the second barrier is microfabricated so as to form a second structure allowing the fluid communication between the outer chamber and the intermediate chamber, and the second structure is different from the first structure.

49. (Canceled).

50. (Currently amended): The bioreactor of claim ~~49~~ 33, wherein the means for electrochemical measurements comprises:

(i) a reference electrode;

(ii) a counter electrode; and

(iii) a plurality of individually addressable working electrodes.

51. (Currently amended): The bioreactor of claim 50, wherein the liquid medium comprises at least one analyte, and wherein the plurality of individually addressable working electrodes comprise a first group of individually addressable working electrodes adapted for ~~capable of~~ sensing the concentration of a single analyte of the liquid medium at multiple locations in the outer chamber or the concentrations of a plurality of analytes of the liquid medium at multiple locations in the outer chamber at a time period shorter than a characterization reaction time related to at least one of cellular physiological activities of the cells.

52. (Currently amended): The bioreactor of claim 51, wherein the first group of individually addressable working electrodes are further adapted for ~~capable of~~ measuring the metabolic variables related to the cells responsive to the liquid medium at multiple locations in the outer chamber at a time period shorter than a characterization reaction time related to at least one of cellular physiological activities of the cells.

53. (Currently amended): The bioreactor of claim 52, wherein the plurality of individually addressable working electrodes comprise a second group of individually addressable working electrodes adapted for ~~capable of~~ sensing the concentration of a single analyte of the liquid medium at multiple locations in the central chamber or the concentrations of a plurality of analytes of the liquid medium at multiple locations in the central chamber at a time period shorter than a characterization reaction time related to at least one of cellular physiological activities of the cells.

54. (Currently amended): The bioreactor of claim 53, wherein the second group of individually addressable working electrodes are further adapted for ~~capable of~~ measuring the metabolic variables related to the cells responsive to the liquid medium at multiple locations in the central chamber at a time period shorter than a characterization reaction time related to at least one of cellular physiological activities of the cells.

55. (Currently amended): The bioreactor of claim 54, wherein the plurality of individually addressable working electrodes comprise a third group of individually addressable working electrodes adapted for ~~capable of~~ sensing the concentration of a single analyte of the liquid medium at multiple locations in the intermediate chamber or the concentrations of a plurality of analytes of the liquid medium at multiple locations in the intermediate chamber at a time period shorter than a characterization reaction time related to at least one of cellular physiological activities of the cells.

56. (Currently amended): The bioreactor of claim 55, wherein the third group of individually addressable working electrodes are further adapted for ~~capable of~~ measuring the metabolic variables related to the cells responsive to the liquid medium at multiple locations in the intermediate chamber at a time period shorter than a characterization reaction time related to at least one of cellular physiological activities of the cells.

57. (Original): The bioreactor of claim 33, wherein the first barrier is substantially circular.

58. (Original): The bioreactor of claim 33, wherein the second barrier is substantially circular.

59. (Original): The bioreactor of claim 33, wherein the boundary is substantially circular.

60. (Currently amended): A bioreactor for cultivating living cells in a liquid medium comprising:

(a) a substrate having a first surface and an opposite second surface, defining a chamber therebetween for receiving the cells and the liquid medium with a boundary; and

(b) means for dividing the chamber into plurality of chambers; and

(c) means adapted for electrochemical measurements of the cells responsive to the liquid medium in at least one of the plurality of chambers,

wherein each of the plurality of subchambers is in fluid communication with at least another one of the plurality of subchambers.

61. (Original): The bioreactor of claim 60, wherein the dividing means comprises a barrier to divide the chamber into a first subchamber and a second subchamber, and wherein the barrier has a porosity to allow the first subchamber and the second subchamber in fluid communication and allow at least one predetermined type of cells to permeate between the first subchamber and the second subchamber.

62. (Original): The bioreactor of claim 60, wherein the dividing means comprises a first barrier and a second barrier to divide the chamber into a first subchamber, a second subchamber and a third subchamber, and wherein the first barrier has a first porosity to allow the first subchamber and the intermediate subchamber in fluid communication and at least a first predetermined type of cells to permeate between the first subchamber and the second subchamber, and the second barrier has a second porosity to allow the second subchamber and the third subchamber in fluid communication and at least a second predetermined type of cells to permeate between the second subchamber and the third subchamber.

63. (Original): The bioreactor of claim 62, wherein the first porosity and the second porosity can be same or different.

64. (Original): The bioreactor of claim 60, wherein the dividing means comprises a plurality of n barriers, n being an integer greater than zero, to divide the chamber into n+1 subchambers.

65. (Original): The bioreactor of claim 64, wherein each of n barriers has a corresponding porosity that can be same or different from that of other barriers.